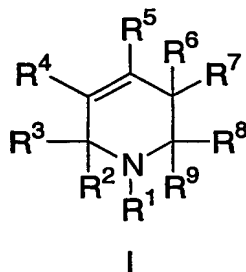


WHAT IS CLAIMED IS:

1. A compound according to Formula I:



5 wherein;

a is 0 or 1;
 b is 0 or 1;
 m is 0, 1, or 2;
 10 n is 0 or 1;
 r is 0 or 1;
 s is 0 or 1;

R¹ is selected from:

- | | |
|----|---|
| 15 | 1) (C ₁ -C ₆ -alkylene) _n (C=X)C ₁ -C ₁₀ alkyl; |
| | 2) (C ₁ -C ₆ -alkylene) _n (C=X)aryl; |
| | 3) (C ₁ -C ₆ -alkylene) _n (C=X)C ₂ -C ₁₀ alkenyl; |
| | 4) (C ₁ -C ₆ -alkylene) _n (C=X)C ₂ -C ₁₀ alkynyl; |
| | 5) (C ₁ -C ₆ -alkylene) _n (C=X)C ₃ -C ₈ cycloalkyl; |
| 20 | 6) (C ₁ -C ₆ -alkylene) _n (C=X)heterocyclyl; |
| | 7) (C ₁ -C ₆ -alkylene) _n (C=X)NR ^c R ^{c'} ; |
| | 8) (C ₁ -C ₆ -alkylene) _n SO ₂ NR ^c R ^{c'} ; |
| | 9) (C ₁ -C ₆ -alkylene) _n SO ₂ C ₁ -C ₁₀ alkyl; |
| | 10) (C ₁ -C ₆ -alkylene) _n SO ₂ C ₂ -C ₁₀ alkenyl; |
| 25 | 11) (C ₁ -C ₆ -alkylene) _n SO ₂ C ₂ -C ₁₀ alkynyl; |
| | 12) (C ₁ -C ₆ -alkylene) _n SO ₂ -aryl; |
| | 13) (C ₁ -C ₆ -alkylene) _n SO ₂ -heterocyclyl; |
| | 14) (C ₁ -C ₆ -alkylene) _n SO ₂ -C ₃ -C ₈ cycloalkyl; |

15) $(C_1-C_6\text{-alkylene})_n P(=O)R^d R^{d'}$;

16) aryl;

17) heterocyclyl; and

18) C_1-C_{10} alkyl;

5 said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, alkylene, heteroaryl and heterocyclyl is optionally substituted with one or more substituents selected from R^{10} ;

R^2 , R^3 , R^6 , R^8 and R^9 are independently selected from:

1) H;

10 2) $(C=O)_r O_s (C_1-C_{10})$ alkyl;

3) $O_r (C_1-C_3)$ perfluoroalkyl;

4) (C_0-C_6) alkylene- $S(O)_m R^a$;

5) oxo;

6) OH;

15 7) halo;

8) CN;

9) $(C=O)_r O_s (C_2-C_{10})$ alkenyl;

10) $(C=O)_r O_s (C_2-C_{10})$ alkynyl;

11) $(C=O)_r O_s (C_3-C_6)$ cycloalkyl;

20 12) $(C=O)_r O_s (C_0-C_6)$ alkylene-aryl;

13) $(C=O)_r O_s (C_0-C_6)$ alkylene-heterocyclyl;

14) $(C=O)_r O_s (C_0-C_6)$ alkylene- $N(R^b)_2$;

15) $C(O)R^a$;

16) (C_0-C_6) alkylene- $CO_2 R^a$;

25 17) $C(O)H$;

18) (C_0-C_6) alkylene- $CO_2 H$;

19) $C(O)N(R^b)_2$;

20) $S(O)_m R^a$; and

21) $S(O)_2 N(R^b)_2$;

30 said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b , OH, (C_1-C_6) alkoxy, halogen, $CO_2 H$, CN, $O(C=O)C_1-C_6$ alkyl, oxo, and $N(R^b)_2$;

R^4 and R^7 are selected from:

35 1) alkyl;

- 2) C₃-C₈ cycloalkyl;
- 3) aryl; and
- 4) heterocyclyl;

said alkyl, cycloalkyl, aryl and heterocyclyl are optionally substituted with up to 3 substituents
5 selected from R¹³;

R⁵ is:

- 1) H;
- 2) C₁-C₁₀ alkyl;
- 10 3) C₂-C₁₀ alkenyl;
- 4) C₂-C₁₀ alkynyl;
- 5) CN;
- 6) halo;
- 7) CO₂H;
- 15 8) (C₁-C₆)alkyl amino; and
- 9) (C₁-C₆)alkyl hydroxy;

R¹⁰ is:

- 1) (C=O)_aO_bC₁-C₁₀ alkyl;
- 20 2) (C=O)_aO_baryl;
- 3) C₂-C₁₀ alkenyl;
- 4) C₂-C₁₀ alkynyl;
- 5) (C=O)_aO_b heterocyclyl;
- 6) CO₂H;
- 25 7) halo;
- 8) CN;
- 9) OH;
- 10) O_bC₁-C₆ perfluoroalkyl;
- 11) O_a(C=O)_bNR¹¹R¹²;
- 30 12) S(O)_mR^a;
- 13) S(O)₂NR¹¹R¹²;
- 14) oxo;
- 15) CHO;
- 16) (N=O)R¹¹R¹²; or
- 35 17) (C=O)_aO_bC₃-C₈ cycloalkyl;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹³;

R¹¹ and R¹² are independently selected from:

- 5 1) H;
- 2) (C=O)O_bC₁-C₁₀ alkyl;
- 3) (C=O)O_bC₃-C₈ cycloalkyl;
- 4) (C=O)O_baryl;
- 5) (C=O)O_bheterocyclyl;
- 10 6) C₁-C₁₀ alkyl;
- 7) aryl;
- 8) C₂-C₁₀ alkenyl;
- 9) C₂-C₁₀ alkynyl;
- 10) heterocyclyl;
- 15 11) C₃-C₈ cycloalkyl;
- 12) SO₂R^a;
- 13) (C=O)NR^b₂;
- 14) oxo; and
- 15) OH;
- 20 said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R¹³; or

R¹¹ and R¹² can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in
 25 addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R¹³;

R¹³ is selected from:

- 30 1) (C=O)_rO_s(C₁-C₁₀)alkyl;
- 2) O_r(C₁-C₃)perfluoroalkyl;
- 3) (C₀-C₆)alkylene-S(O)_mR^a;
- 4) oxo;
- 5) OH;
- 35 6) halo;

- 7) CN;
- 8) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_2\text{-C}_{10})\text{alkenyl}$;
- 9) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_2\text{-C}_{10})\text{alkynyl}$;
- 10) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_3\text{-C}_6)\text{cycloalkyl}$;
- 11) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_0\text{-C}_6)\text{alkylene-aryl}$;
- 12) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_0\text{-C}_6)\text{alkylene-heterocyclyl}$;
- 13) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_0\text{-C}_6)\text{alkylene-N(R}^b)_2$;
- 14) C(O)R^a ;
- 15) $(\text{C}_0\text{-C}_6)\text{alkylene-CO}_2\text{R}^a$;
- 16) C(O)H ;
- 17) $(\text{C}_0\text{-C}_6)\text{alkylene-CO}_2\text{H}$;
- 18) $\text{C(O)N(R}^b)_2$;
- 19) $\text{S(O)}_m\text{R}^a$; and
- 20) $\text{S(O)}_2\text{N(R}^b)_2$;

15 said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b , OH, $(\text{C}_1\text{-C}_6)\text{alkoxy}$, halogen, CO_2H , CN, $\text{O}(\text{C}=\text{O})\text{C}_1\text{-C}_6$ alkyl, oxo, and $\text{N(R}^b)_2$;

R^a is $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_3\text{-C}_6)\text{cycloalkyl}$, aryl, or heterocyclyl;

20 said alkyl, cycloalkyl, aryl or heterocyclyl is optionally substituted with one or more substituents selected from R^f ;

R^b is H, $(\text{C}_1\text{-C}_6)\text{alkyl}$, aryl, heterocyclyl, $(\text{C}_3\text{-C}_6)\text{cycloalkyl}$, $(\text{C}=\text{O})\text{OC}_1\text{-C}_6$ alkyl, $(\text{C}=\text{O})\text{C}_1\text{-C}_6$ alkyl or $\text{S(O)}_2\text{R}^a$;

25 said alkyl, cycloalkyl, aryl or heterocyclyl is optionally substituted with one or more substituents selected from R^f ;

R^c and $\text{R}^{c'}$ are independently selected from: H, $(\text{C}_1\text{-C}_6)\text{alkyl}$, aryl, heterocyclyl and $(\text{C}_3\text{-C}_6)\text{cycloalkyl}$, optionally substituted with one, two or three substituents selected from R^{13} , or

30 R^c and $\text{R}^{c'}$ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 4-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents
35 selected from R^{13} ;

R^d and $R^{d'}$ are independently selected from: (C₁-C₆)alkyl, (C₁-C₆)alkoxy and NR^{b_2} , or

R^d and $R^{d'}$ can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 4-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from NR^e , O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from R^{13} ;

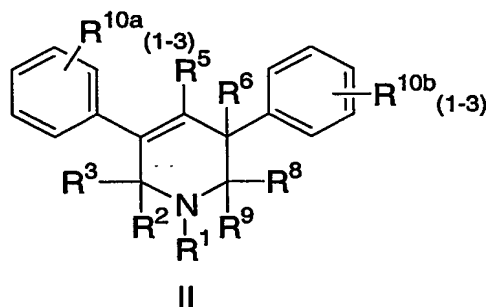
R^e is selected from: H and (C₁-C₆)alkyl;

R^f is selected from: heterocyclyl, amino substituted heterocyclyl, (C₁-C₆)alkyl, amino (C₁-C₆)alkyl, (C₁-C₆)alkyl amino, hydroxy (C₁-C₆)alkyl, OH and NH₂; and

X is selected from O, NR^e and S;

or a pharmaceutically acceptable salt or stereoisomer thereof.

2. The compound according to Claim 1, as illustrated by Formula II:



wherein:

R^{10a} and R^{10b} are independently selected from:

- 1) H;
- 2) C₁-C₁₀ alkyl;
- 3) C₂-C₁₀ alkenyl;
- 4) C₂-C₁₀ alkynyl;
- 5) OH;
- 6) CN;

- 7) halo;
- 8) CHO;
- 9) CO₂H;
- 10) (C₁-C₆)alkyl amino; and
- 11) (C₁-C₆)alkyl hydroxy;

and all other substituents and variables are as defined in Claim 1;

or a pharmaceutically acceptable salt or stereoisomer thereof.

3. The compound according to Claim 2 wherein:

R¹ is selected from:

- 1) (C₁-C₆-alkylene)_n(C=X)C₁-C₁₀ alkyl;
- 2) (C₁-C₆-alkylene)_n(C=X)aryl;
- 3) (C₁-C₆-alkylene)_n(C=X)C₂-C₁₀ alkenyl;
- 4) (C₁-C₆-alkylene)_n(C=X)C₂-C₁₀ alkynyl;
- 5) (C₁-C₆-alkylene)_n(C=X)C₃-C₈ cycloalkyl;
- 6) (C₁-C₆-alkylene)_n(C=X)heterocyclyl;
- 7) (C₁-C₆-alkylene)_n(C=X)NR^cR^{c'};
- 8) (C₁-C₆-alkylene)_nSO₂NR^cR^{c'};
- 9) (C₁-C₆-alkylene)_nSO₂C₁-C₁₀ alkyl;
- 10) (C₁-C₆-alkylene)_nSO₂-aryl;
- 11) (C₁-C₆-alkylene)_nSO₂-heterocyclyl;
- 12) (C₁-C₆-alkylene)_nSO₂-C₃-C₈ cycloalkyl;
- 13) (C₁-C₆-alkylene)_nP(=O)R^dR^{d'};
- 14) aryl;
- 15) heterocyclyl; and
- 16) C₁-C₁₀ alkyl;

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, alkylene, heteroaryl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

and all other substituents and variables are as defined in Claim 2;

or a pharmaceutically acceptable salt or stereoisomer thereof.

4. The compound according to Claim 3 wherein:

R¹ is selected from:

- 5 1) (C=O)C₁-C₁₀ alkyl;
- 2) (C=O)aryl;
- 3) (C=O)C₂-C₁₀ alkenyl;
- 4) (C=O)C₂-C₁₀ alkynyl;
- 5) (C=O)C₃-C₈ cycloalkyl;
- 10 6) (C=O)NR^cR^{c'};
- 7) SO₂NR^cR^{c'};
- 8) SO₂C₁-C₁₀ alkyl;
- 9) SO₂-aryl;
- 10) SO₂-heterocyclyl;
- 15 11) SO₂-C₃-C₈ cycloalkyl; and
- 12) P(=O)R^dR^{d'};

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, alkylene, heteroaryl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

20 R², R³, R⁶, R⁸ and R⁹ are independently:

- 1) H;
- 2) C₁-C₁₀ alkyl;
- 3) C₂-C₁₀ alkenyl;
- 4) C₂-C₁₀ alkynyl;
- 25 5) CHO;
- 6) CO₂H;
- 7) (C₁-C₆)alkyl amino;
- 8) (C₁-C₆)alkyl hydroxy;
- 9) (C=O)_rO_s(C₁-C₁₀)alkyl; and
- 30 10) C(O)N(R^b)₂;

R⁵ is:

- 1) H;
- 2) (C₁-C₆)alkyl amino; and
- 35 3) (C₁-C₆)alkyl hydroxy;

and all other substituents and variables are as defined in Claim 3;

or a pharmaceutically acceptable salt or stereoisomer thereof.

5

5. The compound according to Claim 4 wherein:

R¹ is selected from:

- 10
- 1) (C=O)NR^cR^{c'};
 - 2) SO₂NR^cR^{c'};
 - 3) SO₂C₁-C₁₀ alkyl; and
 - 4) (C=O)C₁-C₁₀ alkyl;

said alkyl is optionally substituted with one, two or three substituents selected from R¹⁰;

15 and all other substituents and variables are as defined in Claim 4;

or a pharmaceutically acceptable salt or stereoisomer thereof.

6. A compound selected from:

20

5-(2,5-difluorophenyl)-N,N-dimethyl-3-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

1-acetyl-5-(2,5-difluorophenyl)-3-phenyl-1,2,3,6-tetrahydropyridine;

25 5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

5-(2,5-difluorophenyl)-N,N-dimethyl-3-phenyl-3,6-dihydropyridine-1(2H)-sulfonamide;

30 (1S)-1-cyclopropyl-2-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-2-oxoethanamine;

5-(2,5-difluorophenyl)-N-methyl-N-(1-methylpiperidin-4-yl)-3-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

5-(2,5-difluorophenyl)-N-[2-(dimethylamino)ethyl]-N-methyl-3-phenyl-3,6-dihydropyridine-1(2H)-carboxamide

5-(2,5-difluorophenyl)-3-phenyl-1-(pyrrolidin-1-ylcarbonyl)-1,2,3,6-tetrahydropyridine

5
5-(2,5-difluorophenyl)-N-(2-hydroxyethyl)-N-methyl-3-phenyl-3,6-dihydropyridine-1(2H)-carboxamide

5-(2,5-difluorophenyl)-1-(2,2-dimethylpropanoyl)-3-phenyl-1,2,3,6-tetrahydropyridine

10
4-[[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]carbonyl]morpholine

4-[[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]acetyl]morpholine

15
2-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-N,N-dimethylacetamide

1-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-2-methyl-1-oxopropan-2-ol

20
N-tert-butyloxycarbonyl-1-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-1-oxopropan-2-amine

1-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-2-methyl-1-oxopropan-2-amine

3-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-3-oxopropan-1-amine

25
1-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-1-oxopropan-2-amine

or a pharmaceutically acceptable salt or stereoisomer thereof.

30
7. A compound selected from:

2-[[[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]carbonyl](methyl)amino]-N,N-dimethylethanaminium trifluoroacetate

35

5-(2,5-difluorophenyl)-1-[2-(dimethylamino)-2-oxoethyl]-3-phenyl-1,2,3,6-tetrahydropyridinium trifluoroacetate

5 5-(2,5-difluorophenyl)-1-[2-(dimethylamino)-2-oxoethyl]-3-phenyl-1,2,3,6-tetrahydropyridinium trifluoroacetate

1-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-2-methyl-1-oxopropan-2-aminium trifluoroacetate

10 3-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-3-oxopropan-1-aminium trifluoroacetate and

1-[5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridin-1(2H)-yl]-1-oxopropan-2-aminium trifluoroacetate.

15

8. The compound according to Claim 6 which is selected from:

5-(2,5-difluorophenyl)-3-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

20 or a pharmaceutically acceptable salt or stereoisomer thereof.

9. A pharmaceutical composition comprising a pharmaceutical carrier, and dispersed therein, a therapeutically effective amount of a compound of Claim 1.

25 10. A method for treating cancer which comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 1.

11. A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

30

12. A process for making a pharmaceutical composition comprising combining a compound of Claim 1 and a pharmaceutically acceptable carrier.

35 13. The composition of Claim 11 further comprising a second compound selected from: an estrogen receptor modulator, an androgen receptor modulator, a retinoid

receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonist, a PPAR- δ agonist; an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle checkpoint, and an apoptosis inducing agent.

14. The composition of Claim 13, wherein the second compound is an angiogenesis inhibitor selected from the group consisting of a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP (matrix metalloprotease) inhibitor, an integrin blocker, interferon- α , interleukin-12, pentosan polysulfate, a cyclooxygenase inhibitor, carboxyamidotriazole, combretastatin A-4, squalamine, 6-O-chloroacetyl-carbonyl)-fumagillol, thalidomide, angiostatin, troponin-1, or an antibody to VEGF.

15. The composition of Claim 13, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

16. A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

17. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a compound selected from: an estrogen receptor modulator, an androgen receptor modulator, retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonists, a PPAR- δ agonist, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle checkpoint, and an apoptosis inducing agent.

18. A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy and a compound selected from: an estrogen receptor modulator, an androgen receptor

modulator, retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonists, a PPAR- δ agonist, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent
5 useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle checkpoint, and an apoptosis inducing agent.

10 19. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.

20. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a COX-2 inhibitor.